

low-temperature aging. At present, not less than 90% of the beer produced in the world is a lager-type beer and, therefore, the bottom fermenting yeast that is used for brewing of the lager-type beer has been most widely used in beer brewing.

[0026] In the so-called fermentation production where production is carried out using a microorganism including the above-mentioned brewing yeast, it is important that the fermentation process is optimized and that the useful strain is selected and bred, in order to increase productivity and improve quality of the product.

[0027] In the case of optimization of beer brewing, there has been conducted a method where an amount of yeast metabolites such as alcohol (e.g. ethanol), ester, organic acid, etc. are monitored, and then temperature, quantity of airflow, content of raw material, etc. are controlled. In such a case, material uptake and excretion by yeast cells and metabolism in the cells are handled as a black box and only very superficial control is carried out. In addition, for the purpose of giving, for example, high flavor to an alcoholic beverage, a process control method for suppressing the amount of oxygen supply during beer brewing or the like has been tried. In such a method, however, growth rate of the yeast itself is reduced due to insufficient oxygen, and adverse effect such as retardation of fermentation and/or deterioration of beer quality may arise. Accordingly, there has been a limit on the improvement in productivity and quality of beer by means of optimization of fermentation processes.

[0028] On the other hand, with regard to a method of breeding useful industrial yeast such as useful beer yeast, a technique for selecting desirable strain has widely been used rather than actual breeding. Beer brewing per se has been performed since well before the discovery of microorganisms by Pasteur. In the beer brewing, a method of selecting more suitable strain of beer yeast from many strains of yeast used in the beer brewery has been traditionally carried out while there have been few cases where beer yeast with good traits is positively bred.

[0029] As an example of a positive breeding method, there is a method where artificial mutagenesis by chemicals or radioactive rays is used. However, brewing yeast, particularly a bottom fermenting yeast which is widely used in beer brewing, is in many cases a polyploid. In that case, it is not possible to produce the desired mutant unless mutation takes place in all of the alleles to be mutated. Accordingly, although it is possible to induce desirable mutation in the case of a haploid laboratory yeast, it is substantially impossible in the case of beer yeast which is a polyploid.

[0030] In recent years, there has been tried a breeding where mutation or cross-breeding is carried out by using spores isolated from bottom fermenting yeast (c.f., for example, Non-Patent Document 1). However, the bottom fermenting yeast is a polyploid, and has complicated chromosome structure. Therefore, isolation of spores having proliferation ability is difficult, and moreover, it is almost impossible to obtain a strain with good traits from them.

[0031] On the other hand, it has recently become possible that desired genes are introduced and expressed in the brewing yeast using a genetic engineering technique, whereby it has become possible to breed yeast with the

desired character by using the results of functional analysis of genes and the genes which have been functionally analyzed. However, as compared with the baker's yeast (*S. cerevisiae*; c.f., for example, Non-Patent Document 2) of which the whole genome sequence is already clarified, the whole genome sequence of the bottom fermenting yeast has not been clarified and there have been only a very few findings about the gene participating in brewing character specific to bottom fermenting yeast and about the function of the said gene in beer brewing.

[0032] In recent years, transcriptome analysis has been conducted using DNA array where DNA fragments or nucleotide oligomers, each of which has a partial sequence of structural gene or internal region of the chromosome are fixed on solid support. For example, Olesen, et al. conducted a comprehensive genetic expression analysis of bottom fermenting yeast during the brewing using GeneFilters (manufactured by Research Genetics Co.) (c.f., for example, Non-Patent Document 3). However, since the whole genome sequence of bottom fermenting yeast has not been clarified yet, it is ambiguous that what gene is monitored for its expression precisely. As a result, such information is quite insufficient to apply to metabolic analysis of bottom fermenting yeast, and to breeding of useful yeast, and to control of beer brewing process.

[0033] At present, the whole genome sequences of more than 100 species of microorganisms have been determined (c.f., for example, Non-Patent Document 6) including *S. cerevisiae*, *Escherichia coli* (c.f., for example, Non-Patent Document 4) and *Mycobacterium tuberculosis* (c.f., for example, Non-Patent Document 5). On the basis of the determined DNA sequences, genes of these microorganisms are identified and function of an enormous number of genes have been predicted without conducting genetic, biochemical and molecular biological experiments. However, industrial yeast such as brewing yeast which has high ploidy and complicated chromosome structure, and thus an assembly (an operation for connecting the DNA sequences) is presumed to be difficult. Therefore, the whole genome sequence of bottom fermenting yeast which contains two different types of genome (c.f., for example, Non-Patent Document 7) has not been reported yet.

[0034] In the production of specific alcohols or alcoholic beverages, there is a technique to increase concentration of sulfite in the product for control of flavor. Sulfite is known as a compound which has anti-oxidative activity, and has been widely used as an antioxidant in the fields of food, beverage and pharmaceuticals, and also in an alcoholic beverage. For example, in the case of wine that requires a long aging period, sulfite plays an important role for the preservation of its quality. It is also known that, in beer brewing, the quality preservation period becomes long in accordance with the increase in concentration of sulfite contained in the product. Thus, when the amount of sulfite in the product is increased, it is possible to prepare a product that has excellent flavor stability and a long quality preservation period.

[0035] The simplest way to increase the amount of sulfite in the product is addition of sulfite. In Japan, so far as wine is concerned, it is permitted by the Ministry of Health, Labor and Welfare to add sulfite to an extent of not more than 350 ppm in terms of residual sulfite concentration. In that case,